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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,801	02/22/2002	Hugo O. Villar	25352-0022	2049

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/082,801	VILLAR ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2004 and 02 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,9 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Summary of Action

1. Acknowledgment is made of USPTO decision to grant applicant's petition to withdraw the notice of abandonment mailed June 29, 2004.

2. The rejection of the claims 1 and 7 under 35 USC 112, first paragraph, is not maintained in light of the amendment.

3. The rejection of the claim 9 under 35 USC 112, second paragraph, is not maintained in light of the amendment.

4. The rejection of the claims 1-4 and 7 under 35 USC 102(b) for anticipation of Radzikowski et al. is not maintained in light of the amendment.

5. Applicant's amendment necessitates a new ground of the rejection(s) in this Office Action.

Status of Application

6. By Amendment filed March 11, 2004, claims 2, 6-8 and 10-11 have been cancelled; claims 1, 3 and 9 have been amended; and claim 12 has been newly added. Claims 1, 3-5, 9 and 12 are currently pending for the prosecution on the merits.

Election/Restrictions

7. Claims 1, 3-5 and 9 are generic to a plurality of disclosed patentably distinct species comprising "an autoimmune disease, infectious, or hyperplasic diseases selected from autoimmune lymphoproliferative syndrome, autoimmune thyroid disease, hypereosinophilia, viral hepatitis, colon carcinoma, breast carcinoma, prostate cancer, neuroblastoma, and glioma".

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species (for example "autoimmune disease", "infectious disease" or "hyperplasic disease", even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Sam Nguyen on February 02, 2005 a provisional election was made to prosecute "hyperplasic disease" as the elected species. Affirmation of this election must be made by applicant in replying to this Office action. The treatment of "autoimmune disease" or "infectious disease" are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Objections

8. Claim 1 is objected to because of the following informalities: Typographical error such as "lymophoproliferative syndrome" is present. It should be corrected as "lymphoproliferative syndrome".

9. Claim 1 is drafted with improper Markush type language. It is suggested to amend "selected from..." to "selected from the group consisting of ...".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3-5, 9 and 12 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The present claim is drawn to a method of treating an autoimmune, infectious, or hyperplasic disease, namely hyperplastic disease such as colon carcinoma, breast carcinoma, prostate cancer, neuroblastoma and glioma, comprising administering the 9-aminoacridine derivatives of the formula.

The instant specification discloses an assay method or in vitro test to determine the activity of the claimed compounds in stimulating Fas-mediate apoptosis or enhancing Fas receptor expression (Examples 3-5). Although the instant specification describes certain in vitro experiments, there is no correlation on this record between in vitro experiments and a practical utility in currently available form for humans or animals. It is not enough to rely on in vitro studies where, as here, a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to utility in humans or animals.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of stimulation of Fas-mediate apoptosis or enhancing Fas receptor expression by the claimed 9-aminoacrdine derivative(s), the skilled artisan cannot envision how to practice the claimed utility. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)* ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 3-5, 9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radzikowski et al. (Acta. Unio. Intern. Contra. Cancerum, 1962, 18, 222-4), Radzikowski et al. (Archivum Immunologiae et Therapiae Experimentalis, 1969, 17(1), 86-88) and Konopa et al. (US 6589961 B2).

Radzikowski teaches the use of 9-aminoacridine derivatives such as 9-(dimethylaminopropylamino)-4-methoxyacridine and 9-(di-methylaminopropylamino)-2-methylacridine) for the treatment of hyperplastic disease such as tumor or cancer in mice (i.e., sarcoma and lymphoma). See Table 2.

Radzikowski teaches 9-aminoacrdine derivatives that are substituted or unsubstituted on the benzene rings of the acridine (e.g., C-6, 15, 19, 25 and 61) that is useful the treatment of hyperplastic disease such as tumor or cancer in mice (i.e., sarcoma, carcinoma and systemic maligancy). Furthermore, the reference teaches 9-aminoacridine derivatives that ethyl group is substituted for methyl group at the last nitrogen of the side chain (e.g., C-101).

Konopa teaches the use of 9-aminoacridine or 9-aminoacridine derivatives as antitumor agent that is useful for the treatment of prostate cancer, colon cancer, lymphoma, breast cancer, leukemia and sarcoma (column 2, lines 18-21).

The teaching of Radzikowski differs from the claimed invention (i) in the treatment of the specific hyperplasic diseases such as colon carcinoma, breast carcinoma, prostate cancer, neuroblastoma and glioma with the claimed compound of the formula, namely 9-[(3-diethylaminopropyl)amino]acridine and, (ii)the combination of other known therapy.

The above references in combination make clear that compounds having 9-aminoacridine as the base structure are useful for as antitumor agent. Furthermore, the above references in combination make also clear that compounds having unsubstitution on the benzene rings of the acridine or ethyl group substitution for methyl group at the last nitrogen of the side chain is old and well known. Therefore, one having ordinary skill in the art would have been motivated to select the claimed compound with the expectation that substitution of ethyl substituent for

methyl in R4 and R5 position or unsubstitution on the benzene rings of the acridine would not significantly alter the analogous properties of the compound of the reference due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055. Furthermore, one having ordinary skill in the art would have expected that the 9-aminoacrdine derivatives of the claimed formula having similar structure as the Konopa (9-aminoacridine as core group) would be useful for the treatment of prostate cancer, colon cancer, breast cancer as well as sarcoma and lymphoma.

With respect to use of "an additional form of therapy", the examiner determines that the addition of known therapy for the treatment of hyperplastic disease to the compounds of the formula which has been known for the treatment of cancer or tumor are well considered within the skill of the artisan. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. *See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).*

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. No Claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

VICKIE KIM
PRIMARY EXAMINER

Brian Kwon